



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Peter Rice et al.
 Serial No. : 09/699,224
 Filed : October 27, 2000
 Confirmation No. : Not Yet Assigned
 For : PEPTIDE MIMICS OF CONSERVED GONOCOCCAL
 EPITOPES COMPOSITIONS USING THEM
 Group Art Unit : 1645
 Examiner : Not Yet Assigned

RECEIVED
 APR 24 2001
 TECHNOLOGY CENTER R3700

New York, New York
 March 2, 2001

Hon. Commissioner for Patents
 Washington, D.C. 20231

RECEIVED
 APR 24

STATEMENT UNDER 37 C.F.R. §§ 1.56 AND 1.97 TECHNOLOGY CENTER R3700

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants make of record the following documents. For the convenience of the Examiner, applicants have enclosed a completed Form PTO-1449 listing these documents:

Articles

Ahearn, J. M., M. B. Fischer, D. Croix, S. Goerg, M. Ma, J. Xia, X. Zhou, R. G. Howard, T. L. Rothstein, and M. C. Carroll. 1996. Disruption of the Cr2 locus results in a reduction in B-1a cells and in an impaired B cell response to T-dependent antigen. Immunity 4:251.

Apicella, M.A., M.A.J. Westerink, S.A. Morse, H. Schneider, P.A. Rice and J.M. Griffiss. 1986. Bactericidal antibody response of normal human serum to the lipooligosaccharide *Neisseria gonorrhoeae*. J. Infect. Dis. 153:520-526.

Anon, R., M. Shapira and C.O. Jacob. 1983. Synthetic Vaccines. J. Immunol. Methods 61: 261-273.

Banerjee A., R. Wang, S. N. Uljon, P. A. Rice, and E. C. Gotschlich. 1998. Identification of the gene (*lgtG*) encoding the lipooligosaccharide β chain synthesizing glucosyl transferase from *Neisseria gonorrhoeae*. Proc. Natl. Acad. Sci. USA 95:10872.

Böttger, E. C., and D. Bitter-Suermann. 1987. Complement and the regulation of humoral immune responses. Immunol. Today 8:261.

Britigan, B.E., M.S. Cohen and P.F. Sparling. 1985. Gonococcal infection: a model of molecular pathogenesis. N. Eng. J. Med. 312:1683-1694.

Brodin, N.T., J. Dahmén, B. Nilsson, L. Messeter, S. Mårtenson, J. Heldrup, H.O. Sjögren and A. Lundblad. 1988. Monoclonal antibodies produced by immunization with neoglycoproteins containing Gal α 1-4 β 1-4G1c β -O and Gal α 1-4 β 1-4G1cNAc β -O residues: useful immunochemical and cytochemical reagents for blood group P antigens and a differentiation marker in Burkitt lymphoma and other B-cell malignancies. Int. J. Cancer. 42:185-194.

Brooks, G.F. and C.J. Lammel. 1989. Humoral immune response to gonococcal infection. Clin. Micro. Rev. 2:S5-S10.

Brossay, L. et al., "Idiotypic and Anti-Anti-idiotypic Antibodies to *Neisseria Gonorrhoeae* Lipooligosaccharides with Bactericidal Activity but No Cross-Reactivity with Red Blood Cell Antigens", J. Immunol., 151, pp. 234-43 (1993).

Burritt, J.B., C.W. Bond, K.W. Doss and A.J. Jesiat. 1996. Filamentous phage display of oligopeptide libraries. Anal. Biochem. 338: 1-13.

CDC. 1991. Pelvic Inflammatory Disease: Guidelines for Prevention and Management. MMWR 40:1-25

CDC. 1982. Sexually transmitted diseases treatment guidelines. MMWR 31:37S-42S 375-425.

CDC. 1984. Chromosomally mediated resistant *Neisseria gonorrhoeae*-United States. MMWR 33:408-410.

CDC Website. 2000. <http://www.cdc.gov/ncidod/dastlr/gcdir/Resist/gisp.html>

- Cohen, I.R., D.S. Kellogg and L.C. Norins. 1969. Serum antibody response in experimental human gonorrhoeae: immunoglobulins G, A and M. Br. J. Ven. Dis. 45:325-327.
- Croix, D. A., J. M. Ahearn, A. M. Rosengard, S. Han, G. Kelsoe, M. Ma, and M. C. Carroll. 1996. Antibody response to a T-dependent antigen requires B cell expression of complement receptors. J. Exp. Med. 183:1857.
- Dempsey, P. W., M. E. D. Allison, S. Akkaraju, C. C. Goodnow, and D. T. Fearon. 1996 C3d of complement as a molecular adjuvant: Bridging innate and acquired immunity. Sciences 271: 348.
- Densen, P., S. Gulati and P.A. Rice. 1987. Specificity of antibodies against *Neisseria gonorrhoeae* that stimulate neutrophil chemotaxis. J. Clin. Invest. 80:78-87.
- Fischer, M. B., M. Ma, S. Goerg, X. Zhou, J. Xia, X. Zhou, R. G. Howard, T. L. Rothstein, E. Kremmer, F. S. Rosen, and M. C. Carroll. 1996. Regulation of the B cell response to T-dependent antigens by classical Pathway complement. J. Immunol. 157:549.
- Glynn, A.A. and M.E. Ward. 1970. Nature and heterogeneity of the antigens of *Neisseria gonorrhoeae* involved in the serum bactericidal reaction. Infect. Immun. 2:162-168.
- Gnehm, H.E., S.I. Pelton, S. Gulati and P.A. Rice. 1985. Characterization of antigens from nontypable *Haemophilus influenzae* recognized by human bactericidal antibodies. J. Clin. Invest. 75:1645-1658.
- Griffiss, H.M., J.P. O'Brien, R. Yamasaki, G.D. Williams, P.A. Rice and H. Schneider. 1987. Physical heterogeneity of Neisserial lipooligosaccharides reflects oligosaccharides that differ in apparent molecular weight, chemical composition, and antigenic expression. Infect. Immun. 55:1792-1800.
- Gulati, S., D.P. McQuillen, J. Sharon, and P.A. Rice. 1996. Experimental Immunization with a Monoclonal Anti-Idiotope Antibody that Mimics the *Neisseria gonorrhoeae* Lipooligosaccharide Epitope 2C7. J. Infect. Dis. 174: 1238-48.
- Gupta, R.K. and G.R. Siber. 1995. Adjuvants for human vaccines--current status, problems and future prospects. Vaccine 13: 1263-1276.
- Gupta, R.K. and G.R. Siber. 1995. Method for quantitation of IgG subclass antibodies in mouse serum by enzyme-linked immunosorbent assay. J. Immunol. Methods 181: 75-81.

Horng, W.J., "Selective Enhancement of a Subpopulation of Anti-*Neisseria gonorrhoeae* Antibodies in Rabbits Through a Reverse Stimulation by Anti-Idiotypic Antibodies", Fed. Amer. Soc. Exp. Biol., 69th Ann. Meet., April 21-26, 1985 (Anaheim, California), Abstract No. 7502, p. 1694.

Jerne, N.K. 1974. Towards a network theory of the immune system. Ann. Immun. Inst. Pasteur. 125C:373-389.

Joiner, K.A., R. Scales, J.A. Warren, M.M. Frank and P.A. Rice. 1985. Mechanism of action of blocking immunoglobulin G for *Neisseria gonorrhoeae*. Clin. Invest. 76:1765-1772.

Kasper, D.L., P.A. Rice and W.M. McCormack. 1977. Bactericidal antibody in genital infection due to *Neisseria gonorrhoeae*. J. Infect. Dis. 135:243-251.

Kennedy, R.C., K. Adler-Storthe, R.D. Henkel, Y. Sanchez, J.L. Melnick and G.R. Dreesman. 1983. Immune response to hepatitis B surface antigen: enhancement by prior injection of antibodies to the idiotypic. Science 221:853-855.

Kennedy, R.C., J.W. Eichberg, R.E. Landford and G.R. Dressman. 1986. Anti-idiotypic vaccine for type B viral hepatitis in chimpanzees. Science 232:220-223.

Kennedy, R.C. et al., BioTechniques, 3, pp. 404-409 (1985).

Kieber-Emmons T. 1998. Peptide mimotopes of carbohydrate antigens. Immunol. Res. 17: 95-108.

Kieber-Emmons, T., R.E. Ward, S. Raychaudhuri, R. Rein and H. Kohler. 1986. Rational design and application of idiotope vaccines. Int. Rev. Immunol. 1:1-26.

Kim, J.J., R.E. Mandrell, H. Zhen, M.A.J. Westerink, J.T. Poolman and J.M. Griffiss. 1988. Electromorphic characterization and description of conserved epitopes of the lipooligosaccharides of group A *Neisseria meningitidis*. Infect. Immun. 56:2631-2638.

Klaus G.G.B., and J. H. Humphrey. 1977. The generation of memory cells I. The role of C3 in the generation of B memory cells. Immunology 33:31.

Lambden, P.R., J.E. Heckels, H. McBride and P.J. Watt. 1981. The identification and isolation of novel pilus types produced by variants of *Neisseria gonorrhoeae* P9 following selection in vivo. FEMS. Microbiol. Lett. 10:339-341.

Lammel, C.J., R.L. Sweet, P.A. Rice, J.S. Knapp, G.K. Schoolnik, D.C. Heilbron and G.F. Brooks. 1985. Antibody-antigen specificity in the immune response to infection with *Neisseria gonorrhoeae*. J. Infect. Dis. 152:990-1001.

- Lowell, G.H., W.R. Ballou, L.F. Smith, R.A. Wirtz, W.D. Zollinger and W.T. Hockmeyer. 1988. Proteosome-lipopeptide vaccines: enhancement of immunogenicity for malaria CS peptides. *Science* 240: 800-802.
- Luo P., M. Agadjanyan, J. Qiu, M.A. Westerink, Z. Steplewski and T. Kieber-Emmons. 1998. Antigenic and immunological mimicry of peptide mimotopes of Lewis carbohydrate antigens. *Mol. Immunol.* 35: 865-879.
- Mandrell, R.E., H. Schneider, M.A. Apicella, W.D. Zollinger, P.A. Rice and J.M. Griffiss. 1986. Antigenic and physical diversity of *Neisseria gonorrhoeae* lipooligosaccharides. *Infect. Immun.* 54:63-69.
- Mandrell, R.E., J.M. Griffiss and B.E. Macher. 1988. Lipooligosaccharides (LOS) of *Neisseria gonorrhoeae* and *Neisseria meningitidis* have components that are immunochemically similar to precursors of human blood group antigens: carbohydrate sequence specificity of the mouse monoclonal antibodies that recognize crossreacting antigens on LOS and human erythrocytes. *J. Exp. Med.* 168:107-126.
- Mandrell, R.E. 1992. Further antigenic similarities of *Neisseria gonorrhoeae* lipooligosaccharides and human glycosphingolipids. *Infect. Immun.* 60:3017-3020.
- McQuillen D. P., S. Gulati, and P. A. Rice. 1994. Complement-mediated bacterial killing assays. *Methods Enzymol.* 236: 137.
- Molina, H., V. M. Holers, B. Li, Y.-F. Fang, S. Mariathasan, J. Goellner, J. Strauss-Schoenberger, R. W. Karr, and D. D. Chaplin. 1996. Markedly impaired humoral response in mice deficient in complement receptors 1 and 2. *Proc. Natl. Acad. Sci. USA* 93 :3357.
- Morse, S.A., S. Stein and J. Hines. 1974. Glucose metabolism in *Neisseria gonorrhoeae*. *J. Bact.* 120:702-714.
- Newhall, W.J., W.D. Sawyer, and R.A. Haak. 1980. Cross-linking analysis of the outer membrane proteins of *Neisseria gonorrhoeae*. *Infect. and Immun.* 28:785-791.
- Nisonoff, A. and E. Lamoyi. 1981. Implications of the presence of an internal image of the antigen in anti-idiotypic antibodies: possible application to vaccine production. *Clin. Immunol. Immunopathol.* 21:397-406.
- Pepys M. B. 1972. Role of complement in induction of the allergic response. *Nature [New Biol]* 273: 157.
- Pepys, M. B. 1974. Role of complement in induction of antibody production in vivo. *J. Exp. Med.* 140:126.

- Rice, P.A. and D.L. Kasper. 1977. Characterization of gonococcal antigens responsible for induction of bactericidal antibody in disseminated infection. J. Clin. Invest. 60:1149-1158.
- Rice, P.A. and D.L. Kasper. 1982. Characterization of serum resistance of *Neisseria gonorrhoeae* that disseminate. J. Clin. Invest. 70:157-167.
- Rice, P.A., H.E. Vayo, M.R. Tam and M.S. Blake. 1986. Immunoglobulin G antibodies directed against protein III block killing of serum resistant *Neisseria gonorrhoeae* by immune serum. J. Exp. Med. 164:1735-1748
- Rice, P.A. 1989. Molecular basis for serum resistance in *Neisseria gonorrhoeae*. Clin. Micro. Rev. 2S:S112-S117.
- Roberts, R.B. 1967. The interaction in vitro between Group B meningococci and rabbit polymorphonuclear leukocytes. J. Exp. Med. 126:795-817.
- Romero, P.J., J.P. Tam, D. Schlesinger, P. Clavijo, P.J. Barr, R.S. Nussenzweig, V. Nussenzweig and F. Zavala. 1988. Multiple T helper cell epitopes of the circumsporozoite protein of *Plasmodium berghei*. Eur. J. Immunol. 18: 1951-1957.
- Ross, S.C. and P. Densen. 1985. Opsonophagocytosis of *Neisseria gonorrhoeae*: interaction of local and disseminated isolates with complement and neutrophils. J. Infect. Dis. 151:33-41.
- Schaaper, W.M., Lu, Y.A., Tam, J.P. and R.H. Melen. 1990. p.765. In: *Peptides: Chemistry, Structure and Biology*. Rivier, I.E. and G.R. Marshall (eds.). ESCOM Science Publishers, Leiden.
- Schoolnik, G.K. and Mietzner, T.A. 1992. Vaccines against gonococcal infections. In: G.C. Woodrow and M.M. Levine (ed.), New Generation Vaccines, Marcel Dekker, Inc. New York, 565-597.
- Schoolnik, G.K. and Z.A. McGee. 1985. Gonococcal vaccine development strategies: summary of the recommendations of a National Institutes of Health vaccine panel. In: G.K. Schoolnik, G.F. Brooks, S. Falkow, C.E. Frasch, J.S. Knapp, J.A. McCutchan and S.A. Morse (ed.), The pathogenic neisseria, ASM, Washington D.C., 329-331.
- Schreiber, J.R., M. Patarawan, M. Tosi, J. Lennon and G.B. Pier. 1990. Anti-idiotypic-induced lipo-oligosaccharide specific antibody response to *Pseudomonas aeruginosa*. J. Immun. 144:1023-1029.

Schreiber, J.R., G.B. Pier, M. Grout, K. Nixon and M. Patawaran. 1991. Induction of opsonic antibodies to *Pseudomonas aeruginosa* mucoid exopolysaccharide by an anti-idiotypic monoclonal antibody. J. Infect. Dis. 164:507-514.

Shinnick, T.M., J.G. Sutcliff, N. Green and R. Lerner. 1983. Synthetic peptide immunogens as vaccines. Annu. Rev. Microbiol. 37: 425-446.

Smith, G.P. and J.K. Scott. 1993. Libraries of peptides and proteins displayed on filamentous phage. Methods Enzymol. 217: 228-257.

Stein, K.E. and T. Soderstrom. 1984. Neonatal administration of idiotypic or anti-idiotypic primes for protection against *Escherichia coli* K13 infection in mice. J. Exp. Med. 160:1001-1011.

Swanson, J. 1982. Colony opacity and protein II compositions of gonococci. Infect. Immun. 37:359-368.

Tramont, E.C., J.C. Sadoff and M.S. Artenstein. 1974. Cross-reactivity of *Neisseria gonorrhoeae* and *Neisseria meningitidis* and the nature of antigens involved in the bactericidal reaction. J. Infect. Dis. 130:240-247.

Tramont, E.C. and J. Ciak. 1978. Antigonococcal antibodies in genital secretions. In: G.F. Brooks, E.C. Gotschlich, W.D. Sawyer and F.E. Young (ed.), Immunobiology of Neisseria gonorrhoeae (ASM, Washington DC), 274-278.

Tramont, E.C., J.W. Boslego, R. Chung, D. McChesney, J. Ciak, J. Sadoff, M. Piziak, C.C. Brinton, S. Wood and J. Bryan. 1985. Parenteral gonococcal pilus vaccine. In: G.K. Schoolnik, G.F. Brooks, S. Falkow, C.E. Frasch, J.S. Knapp, J.A. McCutchan and S.A. Morse. (eds.), The pathogenic neisseria. (ASM, Washington DC), 316-322.

Tramont, E.C. 1989. Gonococcal vaccines. Clin. Micro. Rev. 2S:S74-S77.

Ward, E.S., D. Güssow, A.D. Griffiths, P.T. Jones and G. Winter. 1989. Binding activities of a repertoire of a single immunoglobulin variable domains secreted from *Escherichia coli*. Nature 341: 544-546.

Ward, M.E., P.R. Lambden, J.E. Heckels and P.J. Ward. 1978. The surface properties of *Neisseria gonorrhoeae*: determinants of susceptibility to antibody complement killing. J. Gen. Micro. 108:205-212.

Ward, M.M., R.E. Ward, J.H. Huang and H. Kohler. 1987. Idiotope vaccine against *Streptococcus pneumoniae*: A precursor study. J. Immunol. 139:2775-2780.

Washington, A.E. 1982. Update on treatment recommendations for gonococcal infections. Rev. Infect. Dis. 4S:S758-S771.

Westerink, M.A., P.C. Giardina, M.A. Apicella and T. Kieber-Emmons. 1995. Peptide mimicry of the meningococcal group C capsular polysaccharide. Proc. Natl. Acad. Sci. USA. 92: 4021-4025.

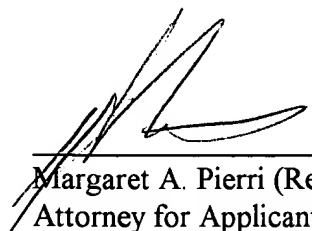
Zavala, F., J.P. Tam, M.R. Hollingdale, A.H. Cochrane, I. Quakyi, R.S. Nussenzweig and V. Nussenzweig. 1985. Rationale for development of a synthetic vaccine against *Plasmodium falciparum* malaria. Science 228: 1436-1440.

Applicants respectfully request (1) that the Examiner fully consider these documents during the course of examination of this application; (2) that the "Notice of References Cited" issued in this application list these documents; and (3) that any patent issuing from the application contain a list of these documents.

This Statement is submitted more than three months from the application filing date but before the mailing date of the first Office Action on the merits. In accordance with 37 C.F.R. § 1.97, submission of this Statement requires no fee. However, if for any reason a fee is due, the Commissioner is hereby authorized to charge payment of any fees required in

connection with this Information Disclosure Statement to Deposit Account No. 06-1075. A duplicate copy of this letter is transmitted herewith.

Respectfully submitted,




Margaret A. Pierri (Reg. No. 30,709)
Attorney for Applicants

S. Craig Rochester (Reg. No. 43,052)
Patent Agent for Applicants

c/o FISH & NEAVE
1251 Avenue of the Americas
New York, New York 10020
Tel.: (212) 596-9000

I Hereby Certify that this
Correspondence is being
Deposited with the U.S.
Postal Service as First
Class Mail in an Envelope
Addressed to: ASSISTANT
COMMISSIONER FOR
PATENTS
WASHINGTON, D.C. 20231 on


Signature of Person Signing